REMARKS

The undersigned submits that he is submitting this response in a representative capacity in accordance with 37 CFR §1.34.

Claims 1-134 are pending in the application, and are herein cancelled. New claims 135-157 are herein presented. No new matter is added by these amendments.

At the outset, Applicants submit herewith new claims 135-157 to replace claims 1-134 including examined claims 1-2, 3, 6-9, 11-14, 16-18, 22, 23-27, 35, 36-39, and 43. As explained in more detail below, Applicants submit that newly presented claims 135-157 are similar to the examined claims, but are rewritten to address the rejections made in the outstanding Office Action and to place the application into better form.

Objections to the Specification

The Examiner objected to the language and format of the Abstract. To overcome this objection, the Applicants herein submit a substitute abstract, and submit that it conforms to the language and format requirements. Accordingly, Applicants submit that this objection is overcome.

The Examiner also objected to the specification because there are allegedly no sequence identifiers for the different sequences given in the Tables. Applicants previously submitted

amendments to add sequence identifiers in the correspondence with the USPTO on February 20, 2001. However, to address the current objection, Applicants submit new Tables that include sequence identifiers and correct several typographical errors. Tables 1 and 2 were resubmitted with sequence identifiers with the substitute sequence listing submitted to the Patent Office on February 27, 2001, and are therefore not included in the present amendment. Applicants submit that no new matter has been added by these amendments. Applicants now submit that this objection has been overcome.

Additionally, the Examiner objected to the specification as allegedly failing to provide proper antecedent basis for the claimed subject matter. Applicants herein amended the specification to incorporate originally filed claims 1 and 2 in the Summary portion of the specification in accordance with MPEP §608.01(o). Applicants submit that the claims are part of the application as filed, no new matter is added by this amendment. Applicants now submit that this objection is overcome.

Rejections under 35 USC §112, first paragraph

Claims 1-3, 6-9, 11-14, 16-18, 22-27, 35-39 and 43 were rejected under 35 USC §112, first paragraph as allegedly failing to comply with the written description requirement.

Specifically, the Examiner alleges that the specification fails to provide an adequate written description of the process steps as claimed. Applicants have amended the specification herein to include the process steps of originally filed claims 1 and 2. Accordingly, Applicants submit that the specification provides an adequate written description of the process steps as claimed.

Additionally the Examiner states that there is no disclosure as to how a method in which a compound can be predicted to modulate a receptor using the claimed method. Applicants respectfully traverse this rejection. Applicants respectfully traverse this rejection.

At the outset, Applicants submit that the application discloses full details of the definition of the panel (page 43 line 6 to page 45 line 15), reference ligands (page 41 line 15 to page 42 line 5), reference conformations (page 31 line 17 to page 32 line 9 and page 42 lines 6-25), reference finger print (page 45 lines 36-39), test substances (page 39 line 30 to page 41 line 15), binding assays (page 59 line 4 - page 74 line 26) and the various types of libraries used in the method (pages 92-95).

Applicants further submit that clear examples have been carried out and are disclosed in the specification of the present application. Applicants wish to draw the Examiner's

attention to Example 1.1 on page 130, which discloses the identification of peptides that bind to unliganded ER-alpha with specific examples listed in Table 1. Additionally, Example 1.2 on page 130 discloses different peptides that bind estradiol activated ER-alpha. This experiment allowed the identification of the LXXLL motif. Applicants also submit that Example 1.3 which discloses the further characterization of peptide sequences and Example 1.4 which discloses the fingerprinting of ER agonists and SERMS are evidence of working examples disclosed in the specification. Applicants submit that the above examples show that binding of peptides can be used to demonstrate agonist activity.

Moreover, Applicants point out Example 2 on pages 135-148. Example 2 discloses actual experimental data and shows fingerprinting of different SERMS with ER-alpha and ER-beta. Further, Examples 3 and 4 demonstrate in vivo fingerprinting, while Example 101 (pages 160-183) confirms the indications of the peptides and shows how different sequences surrounding the motifs can affect their interaction with different receptors. Applicants therefore submit that a considerable amount of experimental work has been carried out with respect to the presently claimed invention. Accordingly, Applicants submit that they were in possession of the necessary information to

allow them to carry out the claimed invention, and that the application does not solely rely on prophetic statements for support.

The Examiner refers to the Valadon reference as proof of the high unpredictability in the art of the present invention. On the contrary, Applicants submit the Valadon reference solves the problems associated with hexapeptide binding. Valadon shows that in 1996 it was known that hexa- and decapeptide motifs could be identified using phage display libraries. In contrast to the Examiner's statement, the Applicants believe the Valadon reference confirms that such libraries could be produced and used by a person of ordinary skill in the art. Even though the reference does refer to some problems with the short insert because flanking regions appear to mask the hexapeptide, it is still clear that it is possible to identify hexamer libraries.

Applicants further submit that Oliphant (cited by the Examiner) was published in 1987 and relates to using recombinant DNA libraries to look for the consensus sequences for *E.coli* promoters. While the success rate was about 1 out of 5 clones with some apparent interference from flanking regions, the paper still shows the method was working. Moreover, Oliphant actually acknowledges that the technique is not difficult (pages 181-182) and suggest ways to improve the success rate. Applicants submit

that Oliphant clearly teaches the skilled person how to address unexpected problems in this technology and reassure the skilled artisan of the likelihood of success.

From the foregoing, it is clear that the present application does not solely rely on prophetic statements to support the invention. Accordingly, the Applicants submit that the current rejection has been overcome and respectfully request the Examiner to withdraw the rejection.

Rejections under 35 USC §112, second paragraph

Claims 1-3, 6-9, 11-14, 16-18, 22-27, 35-39 and 43 were rejected under 35 USC §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner states that the process step (a) contains numerous and allegedly unnecessary steps, and that use of different terminology such as "compound," "test substances" and "plurality of members" to mean the same or different things make the claim confusing. Additionally, claims 3 and 14 were indicated to lack antecedent basis with respect to "ligand" and "the first combinatorial library" respectively.

Applicants submit that newly presented claims 135-157 address these rejections and that these rejections are now overcome.

Double Patenting Rejections

Claims 1, 9 and 23 were rejected under 35 USC §101 as claiming the same invention as that of claims 1 and 6 of prior U.S. Patent No. 6,617,114 (the '114 patent). Applicants respectfully traverse the rejection.

Applicants submit that the test for double patenting under 35 USC §101 is whether a claim in the application could be literally infringed without literally infringing a corresponding claim in the patent. MPEP §804. In other words, the relevant inquiry is whether there is there an embodiment of the invention that falls within the scope of one claim, but not the other? If there is such an embodiment, then identical subject matter is not defined by both claims and statutory double patenting would not exist.

Applicants submit that the '114 patent claims a method to identify ligands which can mediate the biological activity of a target protein via inhibition of the binding of a target protein to a binding partner ligand. In step (a) of claim 1 of the '114 patent, a first combinatorial library is screened to identify

target-binding peptides. Those peptides are used in step (b) to identify ligands that inhibit the binding of target-binding peptides.

In contrast, claim 135 of the present invention now recites forming a reference fingerprint from panel members (usually peptides) and known modulators of the biological activity of a receptor (step 1), forming a test fingerprint from an unknown compound (usually an suspected agonist or antagonist of the receptor) and the same panel members (step 2), and comparing the test fingerprint and the reference fingerprint to predict the receptor modulating activity of the test compound (step 3).

Applicants submit that the invention claimed in the present application is clearly distinguishable from the invention claimed in the '114 patent. The '114 patent does not claim forming a test fingerprint as explicitly recited in the claims of the present invention. The '114 patent does not claim forming a reference fingerprint using a test substance as explicitly recited in the claims of the present application. Moreover, the '114 patent does not claim any type of comparison between a reference fingerprint and a test fingerprint. On this basis, Applicants submit that clearly there is an embodiment of the present invention that falls outside the scope of the claims of the '114 patent. Accordingly, Applicants submit that the

presently claimed invention is not the same as that claimed in the '114 patent, and therefore this rejection is overcome.

Claims 1-3, 6-9, 11-14 and 16 were rejected under the judicially created (nonstatutory) doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2 and 6 of U.S. Patent No. 6,617,114. Claims 1-3, 6-9, 11-14 and 16 were also rejected as being obvious over the '114 patent. Applicants respectfully traverse the rejection.

Obviousness-type double patenting requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent. A double patenting rejection of the obviousness-type is analogous to a failure to meet the nonobviousness requirement of 35 USC §103 except that the patent principally underlying the double patenting rejection is not considered prior art. Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 USC §103 obviousness determination. MPEP §804.

For the reasons outlined above, Applicant submit that the invention claimed in the present application is clearly

distinguishable and not obvious in view of the invention disclosed and claimed in the '114 patent. Accordingly, Applicants submit that the presently claimed invention is not the same as that claimed in the '114 patent, and that this rejection be withdrawn.

In addition, claims 1 and 2 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatenable over claims 27 - 29, 32, 35 and 37 of each of the copending and commonly owned Application Nos. 09/860,688; 10/322,708 and 10/346,162.

Applicants submit that Application No. 09/860,688 is presently abandoned. Therefore, this application will never give rise to an unjustified extension of the granted patent rights because no patent will arise from the '688 application. Accordingly, Applicants request that this rejection, as it applies to Application No. 09/860,688, be withdrawn.

Application Ser. No. 10/322,708 is currently pending, but the Applicants intend to take no further action and allow this application to become abandoned. Such abandonment will become effective April 4, 2005. Accordingly, Applicants respectfully request that this rejection, as it applies to Application No. 10/322,708, be withdrawn in the next office action.

With regard to Application No. 10/346,162 Applicants will submit a suitable Terminal Disclaimer upon indication of allowable subject matter in the present application.

Rejections under 35 USC §102

Claims 1-3, 6-7, 11-14, 18 and 35 were rejected under 35 USC §102(b) as being anticipated by U.S. Patent No. 5,587,293 to Kauvar et al. (Kauvar I) or Kauvar et al. (Current Biology) (Kauvar II). Applicants respectfully traverse this rejection.

Kauvar I discloses a method to determine reactivity of a candidate compound with a target receptor. The method uses a plurality of different target "reference" receptors to which the reactivity or binding of a number of known compounds is determined to produce a table showing the reactivity of the known compounds against each of the receptors. In Kauvar I, an unknown compound is tested against the reference receptors to allow a predicted activity against a target receptor had the target receptor itself been used.

Kauvar II discloses essentially the same method as Kauvar I but uses 8 different proteins as the reference panel.

In contrast, the present invention as recited in new claim 135 requires that the same receptor be assayed in a plurality of different conformations with different reference substances to

produce different fingerprint for each substance. Applicants submit that Kauvar I and Kauvar II differ from the present invention in that Kauvar I and Kauvar II use different reference receptors (isozymes exemplified in Example 1 and at col. 4, lines 46-67) each in a single conformation, whereas the current invention requires that the same receptor be assayed in a plurality of different conformations with different reference substances.

Accordingly, Applicants submit that since the presently claimed features of the same receptor being assayed in a plurality of different conformations with different reference substances to produce different fingerprint for each substance are not disclosed by either Kauvar I or Kauvar II, these reference do not anticipate the presently claimed invention. Accordingly, Applicants submit that this rejection is overcome.

Claims 1-3, 6-7, 11-14, 18 and 35 are rejected under 35 USC §102(e) as being anticipated by U.S. Patent No. 6,255,059 to Klein et al. Applicants respectfully traverse this rejection.

Klein et al. disclose a yeast expression library to identify polypeptides which induce or antagonize receptors. Klein et al used yeast cells containing a target receptor and expressible recombinant genes encoding a peptide library to identify peptides which can modulate the target receptor. At

col. 8, lines 53-67, a peptide library is screened for peptides which potentiate a response on the receptor, and the identified compounds such as peptides are screened to see if they modulate the activity of the active peptides identified in the first screen.

Applicants respectfully submit that the present invention is neither anticipated by nor rendered obvious by Klein et al. As mentioned above, the claimed invention requires that the same receptor to be assayed in a plurality of different conformations with different reference substances to produce different fingerprints for each substance. Applicants submit that Klein et al. does not teach or suggest the presently disclosed and claimed invention. Accordingly, Applicants submit the present is not anticipated by Klein et al, and that this rejection is overcome.

Rejections under 35 USC §103

Claims 1-3, 6-9, 11-14, 16-18, 22-27, 35-39 and 43 were rejected under 35 USC §103(a) as being unpatentable over Kauvar I or Kauvar II in view of U.S. Patent No. 5,723,291 to Kushner et al. or applicants' disclosure of known prior art. Applicants respectfully traverse this rejection.

Kauvar I and II are discussed above. Kushner et al. discloses novel assay methods for identifying compounds that may have both estrogen agonist and antagonist properties. In particular, Kushner et al. disclose assays that use cells comprising promotors having an AP1 site linked to a reporter gene, and compounds capable of inducing or blocking expression of the reporter gene can therefore be identified.

In contrast, the presently disclosed and claimed invention relates to a method of predicting the receptor-modulating activity of a compound that modulates the biological activity of a receptor. Applicants submit that the disclosures of Kauvar I and II taken with Kushner et al. do not disclose or suggest a method of predicting the receptor-modulating activity of a compound that modulates the biological activity of a receptor.. Applicants further submit there is no suggestion in the references cited to combine a method to determine reactivity of a candidate compound with a target receptor from Kauvar I and II and estrogen receptors activate transcription by interaction with another response element, the AP-1 binding site, instead of binding to EREs from Kushner et al. to form the present invention. Accordingly, Applicants submit this rejection has been overcome.

Applicants now submit that the application is in condition for allowance, and reconsideration and a timely Notice of Allowance is earnestly solicited.

If the Examiner believes a telephone conference would aid in the continued prosecution of this application, the Examiner is invited and encouraged to contact Applicants' representative at the telephone number listed below.

Any fees due with this Reply may be charged to Deposit Account **23-1665** under Customer Number **27267**.

Respectfully submitted,

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